IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

ARBUTUS BIOPHARMA CORP. and GENEVANT SCIENCES GMBH, Plaintiffs, v. PFIZER INC. and BIONTECH SE, Defendants.	Civil Action No. 3:23-1876-ZNQ-TJB *Document Filed Electronically* Jury Trial Demanded

PLAINTIFFS' RESPONSIVE MARKMAN BRIEF

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I. INTRODUCTION

Rather than propose constructions that comport with the intrinsic evidence, Defendants offer strained interpretations of the claims to advance their non-infringement positions. They attempt to limit the full scope of the claim terms by importing limitations from the specification into the claims, misinterpreting the intrinsic evidence to argue disclaimer where there is none, and relying on inapplicable caselaw. The Court should reject Defendants' positions and adopt Plaintiffs' constructions.

II. ARGUMENT

A. "Lipid Vesicle" / "Vesicle" ('651 Patent, '320 Patent, '098 Patent)

Defendants' proposed construction for "vesicle" improperly narrows the express definition of lipid vesicle. Defendants attempt to limit the term "vesicle" to mean "a sac containing an aqueous interior or a relatively disordered lipid mixture" based on the exemplary embodiments taught in the specification. In so doing, Defendants ignore the "including, but not limited to" language that clearly identifies the exemplary embodiments as non-limiting. Defendants' construction thus conflicts with the intrinsic evidence and should be rejected.

1. Defendants' Construction Conflicts With The Specification's Explicit Definition And Its Use Of The Words "Including, But Not Limited To"

Defendants criticize Plaintiffs for "rely[ing] on only the first clause of the definition" and "disregard[ing] the rest." Defs' Br. at 11, 14. But Plaintiffs' construction is the full definition of "lipid vesicle" as shown below in the underlined language:

> "Lipid vesicle" refers to **any lipid composition that can be used to deliver a compound** including, **but not limited to**, liposomes, wherein an aqueous volume is encapsulated by an amphipathic lipid bilayer; or wherein the lipids coat an interior comprising a large molecular component, such as a plasmid, with a reduced aqueous interior; or lipid aggregates or micelles, wherein the encapsulated component is contained within a relatively disordered lipid mixture.

'651 patent at 5:30-37 (emphases added). The remainder of the sentence provides non-limiting examples of such compositions, which is made clear by the introductory phrase "including, but not limited to." Defendants' proposed construction effectively deletes the words "any" and "but not limited to" from the specification and changes it to read: "'*Lipid vesicle' refers to* ~~any~~ ***only the following*** *lipid compositions that can be used to deliver a compound ....*"

Defendants' attempt to ignore the "but not limited to" language conflicts with Federal Circuit case law. In *e2Interactive, Inc. v. Blackhawk Network, Inc.*, the court construed the claim term "transaction types." 689 F. App'x 957, 962 (Fed. Cir. 2017). The patent specification disclosed four exemplary transaction types, using the language "include[s] but [is] not limited to." *Id.* at 963 (alteration in original). The court concluded that "the disclosed embodiments are exemplary only and are non-limiting to the scope of 'transaction type.'" *Id.* Similarly, in *Ancora Techs., Inc. v. Apple, Inc.*, the patent at issue provided non-limiting examples of the claim term "program" and referred to certain embodiments as a "non-limiting example." 744 F.3d 732, 735 (Fed. Cir. 2014). The Court rejected the Defendants' attempt to limit the claim term to the examples, noting that the "only instances in which the specification discusses using the claimed invention to verify application programs are found in examples that the specification makes clear are not limiting." *Id.*

These cases are consistent with the well-settled principle that embodiments should not be imported from the specification into the claims. "[O]ne of the cardinal sins of patent law—reading a limitation from the written description into the claims…although the specification often describes very specific embodiments of the invention, we have repeatedly warned against confining the claims to those embodiments." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1323 (Fed. Cir. 2005) (en banc) (citation omitted).

2. Defendants' Cases Involve Claim Language (e.g., "Such As") That The Federal Circuit Has Determined To Be Limiting

Defendants do not cite any cases where the court limited a claim term based on examples described as "non-limiting" or disclosed with the language "but not limited to." Instead, Defendants cite cases where the specification uses the words "such as," "etc." and "are," which courts have interpreted to be limiting language. Defs' Br. at 11-12. There is no such limiting language in the '651 patent's description of the exemplary embodiments of "lipid vesicle." Defendants' cases are thus all inapposite.

In *Int'l Bus. Machines Corp. v. Iancu*, the patent at issue defined the term "entities" to be "a set of distinct entities, **such as** enterprises, organizations, institutions, **etc.**, that cooperate to provide a single-sign-on, ease-of-use experience to a user." 759 F. App'x 1002, 1006 (Fed. Cir. 2019) (emphases added). Based on the specification's use of "such as" and "etc.," the court determined that "entity" was limited to the disclosed exemplary items and "things of a type similar to the itemized ones." *Id.* at 1007. The court recognized that those phrases sometimes limit the scope of a defined term:

> [T]his passage refers to entities "such as" the ones listed and includes "etc."—both of which, in this context, indicate that only things of a type similar to the itemized ones are covered, namely, other establishments or ventures or firms or the like. We have recognized that "such as" and "etc." sometimes have just that meaning.

Id. *US v. Nichols Copper Co*, 29 C.C.P.A. 186 (1941), is distinguishable on the same grounds. In *Nichols*, the court ruled that "the use of the words **'such as'**" in a paragraph of the tariff act means that "a substance not specifically named in the paragraph is like or similar to, or belongs to the same class as, the substances therein named." *Id.* at 191 (emphasis added). Unlike the situations in *IBM,* and *Nichols*, Plaintiffs here did not use the terms "such as" or "etc." to describe the exemplary embodiments. To the contrary, Plaintiffs expressly used the non-limiting language "including, but not limited to."

Defendants' reliance on *Astrazeneca AB, Aktiebolaget Hassle, KBI-E, Inc. v. Mut. Pharm. Co.*, 384 F.3d 1333 (Fed. Cir. 2004) is also misplaced. Defs' Br. at 13. There, the court limited the term "solubilizer" to only surfactant compounds. *Id.* at 1341. The patentee, however, limited the term by using the word "are," rather than using the words "can be" or "includes, but is not limited to." The patent at issue explicitly stated that "**solubilizers suitable** for the preparations according to the invention **are** semi-solid or liquid non-ionic **surface active agents**." *Id.* (emphases added). The court explained that "surface active agents" are "also known as 'surfactants.'" *Id.* at 1336. Thus, the patentee intentionally limited the solubilizers to those that "are" surfactants. As with *IBM* and *Nichols,* the *Astrazeneca* case did not involve the language "but not limited to." Here, the specification does not limit the lipids vesicles to those that "are" one of three exemplary embodiments. To the contrary, the specification states "[l]ipid vesicles" are "not limited to" the disclosed embodiments. '651 patent at 5:30-37.

The string of lexicography cases that Defendants cite are irrelevant, Defs' Br. at 14, because Plaintiffs' construction is based on the express definition of "lipid vesicle," which is consistent with, not a departure from, the plain and ordinary meaning of the term.[1]

3. The Only Expert Testimony Of Record Supports Plaintiffs' Construction

Plaintiffs submitted a declaration from Dr. Thompson, an expert in the delivery of therapeutic agents using lipid particles, with their opening brief. Dr. Thompson did not provide an opinion on the definition of the term "lipid vesicle" in his declaration, because there was no need

[1] The express definition of a claim term controls, even where lexicography is not invoked. *See, e.g., Vasudevan Software, Inc. v. MicroStrategy, Inc.*, 782 F.3d 671, 679 (Fed. Cir. 2015) (applying the prosecution history's definition of a claim term where the definition's "meaning does not conflict with the plain and ordinary meaning of the term"); *Chevron U.S.A. Inc. v. Univ. of Wyoming Rsch. Corp.*, 978 F.3d 1361, 1367 (Fed. Cir. 2020) (affirming claim construction that was "consistent with, and indeed tracks a verbatim definition set forth in, the '814 application").

in view of the express definition in the specification. Nevertheless, during his deposition, Defendants' counsel repeatedly asked for Dr. Thompson's views on "lipid vesicle," including his views on the portion of the specification containing the definition of the term and the exemplary embodiments ('651 patent at 5:30-44), in an attempt to elicit testimony supporting their limited construction of the term. Ex. 1 (Thompson Tr.) at 50-51, 63-67, 79-88. Plaintiffs followed up on Defendants' repeated questions during re-direct examination. Ex. 1 (Thompson Tr.) at 175-185.

To the extent Defendants rely on Dr. Thompson's testimony, that testimony further supports Plaintiffs' position. Courts assess the intrinsic evidence from the viewpoint of a POSA. *See Phillips,* 415 F.3d at 1313. Here, the only evidence of how a POSA would read the specification comes from Dr. Thompson. He testified that a POSA reviewing the '651 patent's specification would understand that "lipid vesicles" were not limited to only the listed examples, just as the specification explicitly states. Ex. 1 (Thompson Tr.) at 180:15-181:7. He further testified that lipid vesicles also included lipid nanoparticles (LNPs), which Defendants contend are not one of the enumerated examples, underscoring that lipid vesicles are not limited to only the discussed embodiments:

> Q: And would a POSA understand that an LNP such as on page 10 of your expert report to be a lipid vesicle in the context of the '651 patent regardless of the amount of water, if any, in the LNP?
>
> …
>
> A: Yes.

Ex 1. (Thompson Tr.) at 183:12-17. Dr. Thompson's testimony thus demonstrates that a POSA reading the patent specification would not consider the examples of "lipid vesicle" to be limiting, contrary to Defendants' position.

B. The "Fully Encapsulated" Terms[2] ('651 Patent, '359 Patent, '378 Patent)

Nine days before this brief was due, Defendants reached out to Plaintiffs offering what they termed a "compromise," specifically, to have the parties agree that the "plain and ordinary meaning" should apply to the two "fully encapsulated" terms—but with no proposed agreement on what is the "plain and ordinary meaning" of the terms. Ex. 2 at 2. During a subsequent meet and confer, Plaintiffs explained that given the parties' dispute as to the "plain and ordinary meaning" of "fully encapsulated," an agreement stating merely that the "plain and ordinary meaning" should apply would not resolve the claim construction dispute. Rather, at trial, the parties would simply present their conflicting views of the "plain and ordinary meaning" to the jury, likely through expert testimony and references to the specification. To do so would improperly convert a claim construction dispute, a matter within the Court's province, into an issue for the jury. *O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co*., 521 F.3d 1351, 1360 (Fed. Cir. 2008) ("When the parties raise an actual dispute regarding the proper scope of these claims, the court, not the jury, must resolve that dispute.").

Two days before this brief was due, Defendants informed Plaintiffs that they were "withdrawing their construction" of this claim term and "maintaining the position that the 'fully encapsulated' term (as used in both families of patents asserted in this case) is indefinite, and thus cannot be defined." Ex. 2 at 1. In their opening brief, however, Defendants argued that the "Molar Ratio patents expressly define the claim phrase 'fully encapsulated'" and offered a construction based on that purported definition. Defs' Br. at 16. Defendants now take issue with their own

[2] Though Plaintiffs address the two patent families together for purposes of this response, Plaintiffs maintain separate proposed constructions as set forth in their opening brief for the two patent families to account for the differing context of the claims in the respective patents. *See* Defs' Br. at 18.

construction and withdraw it, but again proposed that the parties agree for plain and ordinary meaning to apply. Ex. 2 at 1.

To the extent Defendants argue that the plain and ordinary meaning should apply, but with no resolution of what the plain and ordinary meaning is, the Court should reject that proposal. There is a live dispute between the parties as to the meaning of "fully encapsulated." The Court should resolve this dispute here rather than allow the parties' experts to later argue what the term means before the jury. As explained below and in Plaintiffs' opening brief, the Court should adopt Plaintiffs' construction.

1. The Specification Of The Molar Ratio Patents (The '359 And '378 Patents) Does Not Expressly Define "Fully Encapsulated"

In their opening brief, Defendants assert that the patentee acted as its own lexicographer in the Lipid Composition Patents[3] and "expressly define[d]" the "fully encapsulated" terms to mean "the active agent or therapeutic agent in the lipid particle is not significantly degraded after exposure to serum or a nuclease or protease assay that would significantly degrade free DNA, RNA, or protein." Defs' Br. at 16. For the reasons set forth in Plaintiffs' opening brief, Defendants' argument should be rejected.

The portion of the specification relied on by Defendants is not a definition at all, which is confirmed by the fact that it is in the "Description of the Embodiments" section several pages ***after*** the "Definitions" section of the patent. *Compare* '359 Patent at 6:45-14:17 *with* 23:6-10. That the inventors did not intend to define the meaning of "fully encapsulated" is also evident by their use of the term "indicates" rather than the clear definitional language used for nearly every term in the "Definitions" section. *See, e.g.*, '359 Patent at 6:48-49 ("refers to"); *id.* at 8:3-4 ("is intended to

[3] Plaintiffs refer to the '359 and '378 patents as the "Lipid Composition Patents" in their opening brief, Pls' Br. at 1, whereas Defendants refer to them as the "Molar Ratio Patents." Defs' Br. at 7.

mean"); *id.* at 10:26 ("as used herein refers to"). *See Medicines Company v. Mylan, Inc.*, 853 F.3d 1296, 1306 (Fed. Cir. 2017) (finding no lexicography where the statement in dispute "depart[ed] from [the] format" used in defining terms: "the defined term in quotation marks, followed by the terms 'refers to' or 'as defined herein."). Defendants cannot have it both ways.[4]

Moreover, Defendants' proposed construction is pulled from the beginning of a passage in the '359 and '378 patent specification that describes multiple aspects of "fully encapsulated" nucleic acids in no specified order. For instance, the final sentence in the passage states "'fully encapsulated' also indicates that the lipid particles are serum-stable, that is, that they do not rapidly decompose into their component parts upon in vivo administration." '359 Patent at 23:21-24 (emphasis added). That statement exhibits the same characteristics as the first sentence cited by Defendants in support of their construction: "setting off the phrase in quotation marks" and describing a potential **benefit** of full encapsulation, not a **definition** of the term. Defs' Br. at 16. As such, this portion of the specification does not constitute a definition at all, let alone a definition "without ambiguity or incompleteness." Thus, Defendants' reliance on *Sinorgchem* is misplaced, Defs. Br. at 16, as the court there found an express definition of "controlled amount" based on an unambiguous statement that "[a] 'controlled amount' of protic material ***is*** an amount up to that which inhibits the reaction of aniline with nitrobenzene . . ." *Sinorgchem Co., Shandong v. ITC*, 511 F.3d 1132, 1136 (Fed. Cir. 2007)(emphasis added). Defendants should not be permitted to manufacture an indefiniteness argument by cherrypicking a single statement from the specification where the inventors did not "explicitly define[] a claim term." *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1380 (Fed. Cir. 2009); *see also Omega Engineering, Inc. v. Raytek*

[4] Defendants are inconsistent in their arguments. Defendants seek to ignore the express definition of "lipid vesicle," Defs' Br. at 11-15, while creating a definitional statement for "fully encapsulated" that does not exist.

Corp., 334 F.3d 1314, 1335-36 & n.6 (Fed. Cir. 2003) (rejecting construction that resulted in invalidation and reversing summary judgment of indefiniteness).

Defendants' assertion that the adopted construction must capture the "very purpose" and "structural capability" of the claimed inventions is unsupported. Defs' Br. at 17. "The court's task is not to limit claim language to exclude particular devices because they do not serve a perceived 'purpose' of the invention." *E-Pass Techs., Inc. v. 3COM Corp.*, 343 F.3d 1364, 1370 (Fed. Cir. 2003); *see also Phillips*, 415 F.3d at 1325 (declining to import a described capability of the claimed invention from the specification into the claims). And despite Defendants' unfounded suggestion that Plaintiffs' proposed construction is overly broad, as further explained below, Plaintiffs' proposed construction is the only one before the court that makes clear what it means for a nucleic acid to ***be*** fully encapsulated. As Plaintiffs explained in their opening brief, setting forth some benefits of a fully encapsulated nucleic acid does not shed any light on what the term actually means.

2. Plaintiffs' Proposed Construction Is Supported By The Weight Of The Intrinsic And Extrinsic Evidence

Defendants do not address the bulk of the intrinsic evidence cited by Plaintiffs, which illustrates that a POSA would understand "fully encapsulated" to refer to the location of the mRNA relative to the claimed lipid vesicles and particles. The specification of the '651 patent contrasts nucleic acids located in the "interior" of the vesicles, with nucleic acids located "within a relatively disordered lipid mixture" of lipid vesicles. Pls' Br. at 6-7. The specification then refers to full encapsulation or partial encapsulation as shorthand for these different states. *See* '651 patent at 5:38-40 ("As used herein, 'lipid encapsulated' can refer to a lipid formulation which provides a

compound with full encapsulation, partial encapsulation, or both[5].”). The Lipid Composition Patents contain similar disclosures. ’359 patent at 11:59-65 (“As used herein, ‘lipid encapsulated’ can refer to a lipid particle that provides . . . with full encapsulation, partial encapsulation, or both.”).

Defendants’ assertion that Plaintiffs’ construction fails to account for the term “fully” as a “modifier for encapsulation” is incorrect. *See* Defs’ Br. at 16. The term “fully” describes the location of the encapsulated nucleic acid as inside the lipid vesicles or particles, as distinguished from “partially” encapsulated nucleic acid where the molecules are merely associated with the surface of those vesicles or particles in a “relatively disordered lipid mixture.” ’651 Patent at 5:30-40; Pls’ Br. at 6-7, 11. For the same reason, Defendants’ argument that “encapsulated” and “contained inside” are not synonymous is irrelevant. Defs’ Br. at 17. Plaintiffs do not contend those terms to be synonymous; Plaintiffs contend “***fully*** encapsulated” means “contained inside.” Defendants have not offered any persuasive reason why that should not be the case aside from vague generalizations that the claims would be “unduly broad.”[6] Defs’ Br. at 16-17.

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[5] “Both” states present in a formulation refers to a formulation that includes some nucleic acids contained inside the lipid vesicles and some nucleic acids located within a relatively disordered lipid mixture.

[6] Defendants’ cases do not suggest otherwise. Defs’ Br. at 17. The quote that Defendants rely on from *Intel Corp. v. Qualcomm Inc,* is unremarkable, as it states merely that a construction should “capture the scope of the actual invention rather than strictly limit the scope of claims to disclosed embodiments or allow the claim language to become divorced from what the specification conveys is the invention.” 21 F.4th 801, 809 (Fed. Cir. 2021). Here, Plaintiffs’ proposed construction is consistent with the specification, which as Defendants acknowledge, describes certain benefits associated with nucleic acids being fully encapsulated. In *Pall Corp. v. Hemasure Inc.*, the court rejected as “unduly broad” a construction that expanded the role of the recited “gas outlet” beyond its purpose. 181 F.3d 1305, 1310 (Fed. Cir. 1999). There is no such overreaching here, as the intrinsic and extrinsic evidence confirms that the location of the nucleic acid is what defines full encapsulation and distinguishes it from partial encapsulation. In *Doorking, Inc. v. Sentex Systems, Inc.*, 19 Fed. App’x 872, 877 (Fed. Cir. 2011), the court rejected a broad interpretation of “disabling” that would sweep in prior art distinguished by the applicant during prosecution.

The prosecution history of the '651 patent further confirms that the "fully encapsulated" limitation was understood to refer to nucleic acids located "within the lipid vesicles of the present invention" as opposed to being "merely associated with the surface" of a preformed vesicle, as in the prior art. *See* Pls' Br. at 7 (discussing how applicant overcame the Unger reference). Defendants do not grapple with any of this intrinsic evidence, and their own background description of lipid particle manufacturing contemplates the very same distinction between full and partial encapsulation that is described by the intrinsic evidence. Defs' Br. at 5 (describing that some nucleic acids may "stick to the exterior of a particle" and some may "be entirely within the particle").

The intrinsic evidence also confirms that the broader phrase Plaintiffs seek to construe in the '651 patent refers to the standard measurement for assessing full encapsulation of a nucleic acid by lipid vesicles known as "encapsulation efficiency." As discussed in Plaintiffs' opening brief, the '651 specification includes several express references to encapsulation efficiency, including ones that describe the very encapsulation percentages claimed, demonstrating that the inventors intended to claim particular encapsulation efficiencies. Pls' Br. at 7-8. And during prosecution of the '651 patent, the applicant and examiner discussed the claims and prior art in terms of encapsulation efficiency—specifically as measured by the standard "fluorescent dye binding assay." Pls' Br. at 8 (discussing applicants overcoming Semple prior art reference by claiming higher encapsulation efficiency). The '359 and '378 patents expressly describe dye binding assays as a method for measuring full encapsulation, demonstrating that they share the same understanding of what it means for a nucleic acid to be fully encapsulated and that

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Plaintiffs' proposed construction here is supported by the prosecution history, whereas Defendants' argument ignores it.

encapsulation efficiency is a measurement of full encapsulation. '359 patent at 23:16-20 ("full encapsulation may be determined by an Oligreen® assay . . ."). Again, Defendants do not cite any evidence to the contrary nor even mention encapsulation efficiency. Defs' Br. at 18 (merely arguing Plaintiffs' proposed construction for the '651 patent should be rejected for the same reasons as the Molar Ratio Patents). Plaintiffs' intrinsic evidence therefore stands unrebutted and is conclusive. *Seabed Geosolutions (US) Inc. v. Magseis FF LLC*, 8 F.4th 1285, 1287 (Fed. Cir. 2021) ("If the meaning of a claim term is clear from the intrinsic evidence, there is no reason to resort to extrinsic evidence.").

Defendants contend that there are multiple methods available to measure full encapsulation and therefore the claims of the '651 patent are indefinite. Not so. Plaintiffs' expert, Dr. Thompson, has explained that a POSA reading the '651 patent would have known to measure the claimed encapsulation efficiencies using a standard fluorescent dye assay. D.I. 84-5 (Thompson Decl.) ¶¶ 55, 60, 69 (citing Zhang 1999; MacLachlan 2007; Heyes 2005; WO 00/03683); Ex. 1 (Thompson Tr.) at 94:10-11 ("Encapsulation efficiency is the proportion of the strands that are initially dye inaccessible."); *id.* at 95:11-15 ("The method that's described in paragraph 69 and the disclosure and specifically the figure legends and throughout the specification refer to encapsulation efficiency. Anyone working in this field knows what that methodology entails."). A POSA would have also understood that such dye assays differentiate between fully encapsulated nucleic acids and partially encapsulated nucleic acids, such as those in the lipoplexes and other disordered mixtures described in the '651 patent. Ex. 1 (Thompson Tr.) at 99:21-100:2 ("The dye will bind to nucleic acid that is exposed. And if there are lipoplex[es] in the sample, those nucleic acids are exposed to the aqueous phase where the dye exists. The dye will bind to those exposed sequences. The dye is incapable of binding to nucleic acids that are fully – that are contained inside a lipid

vesicle."); *id.* at 101:6-11; *id.* at 103:14-16 ("Partial encapsulation is what I'm referring to here, partial meaning that it's within disordered lipid mixture and is dye accessible.").[7]

Defendants have provided no expert testimony and thus the extrinsic evidence, like the intrinsic evidence, stands unrebutted in Plaintiffs' favor. *Lippert Components Mfg., Inc. v. Morryde Int'l Inc.*, No. 3:16-CV-264 JD, 2018 WL 3957203, at *5 (N.D. Ind. Aug. 17, 2018) ("Such unrebutted evidence shall be credited, to the extent it is not conclusory or at odds with the intrinsic evidence….").

For these reasons, and those set forth in Plaintiffs' opening brief, the Court should adopt Plaintiffs' constructions and construe "wherein at least 70% / at least 80% / about 90% of the mRNA in the formulation is fully encapsulated in the lipid vesicles" in the claims of the '651 patent to mean "wherein at least 70% / at least 80% / about 90% of the mRNA in the formulation is contained inside the lipid vesicles.[8] Similarly, the Court should construe "fully encapsulated" in the claims of the '359 and '378 patents to mean "contained inside."

C. Mol % Terms ('359 Patent)

Defendants assert that the conventional rules of rounding do not apply to the numbers recited in the claims, such that "50" must be construed to mean "50.000" or an even more precise number with infinite trailing zeros. However, Federal Circuit precedent, the intrinsic record, and

[7] To the extent Defendants contend partial encapsulation does not refer to the lipid aggregates or similar disordered systems described in the '651 patent but rather situations where a nucleic acid molecule is partially inside and partially outside the lipid vesicle or particle, such an interpretation is not supported by the intrinsic or extrinsic evidence. Neither patent specification mentions half-in, half-out molecules. Dr. Thompson has also rejected the theory as scientifically unsound. Ex. 1 (Thompson Tr.) at 60:6-61:3 (testifying he has never observed nucleic acids that are "half-inside, half-outside of the particle" and describing them as "not a state that is thermodynamically stable").

[8] Plaintiffs' opening brief contained a typographical error in the proposed construction "wherein at least 70% / at least 80% / about 90% of the mRNA is in the formulation is contained inside the lipid vesicles." The underlined "is" should be removed in the construction if adopted, as reflected in the parties' Joint Claim Construction and Prehearing Statement. Dkt. 66-1 at 9.

expert testimony uniformly support Plaintiffs' construction of the claimed mol % ranges to have their plain meaning in accordance with the rules of significant figures and rounding. The Federal Circuit has repudiated Defendants' argument that the lack of broadening language means that strict numerical boundaries must be applied. The lone rounding case that Defendants rely on is also readily distinguishable. And contrary to Defendants' argument, the removal of "about" from the asserted claims during prosecution of a related patent was unrelated to rounding and certainly did not demonstrate a clear and unmistakable disclaimer of rounding.

Defendants' arguments suffer from the erroneous presumption that the plain meaning of a number includes additional zeros beyond the number of stated significant digits. According to Defendants' position, the plain meaning of "50"—stated to two significant digits—is the same as stating "50.000" or even "50.000000." To the contrary, however, the plain meaning of "50," in accordance with the standard rounding convention, literally encompasses values of "49.5 to $50.4\overline{9}$" because those values round exactly to "50" when stated to the number of significant digits in "50" (*i.e.*, two). Rounding does not alter the number at issue, nor does it depend on words of broadening such as "about" or "approximately." The literal meaning of a number includes those numbers that fall within the standard scope of rounding.

A POSA would have understood from the specification and prosecution history at issue here that the standard rules of rounding apply to the claimed ranges. This position is supported by the testimony of Plaintiffs' expert, Dr. Thompson. D.I. 84-5 (Thompson Decl.) ¶ 75-92. Dr. Thompson's testimony is uncontested as Defendants did not provide a contrary supporting expert declaration with their opening brief.[9]

[9] Defendants should be precluded from any attempt to offer expert testimony with their responsive brief. Defendants have been on notice of Plaintiffs' claim construction position and intention to

1. Defendants Rely On Inapplicable Caselaw

Defendants argue "[w]hen confronted with exact ranges without words of broadening, courts apply the endpoints as strict numerical boundaries." Defs' Br. at 19. Defendants' argument begs the question. The issue is not whether the endpoints are "strict numerical boundaries." The issue is what values fall within the plain meaning of the numerical boundary at each end of the range.

Defendants obfuscate the dispute between the parties by relying on *Cobalt Boats*, *Jeneric*, and *Takeda*, none of which relate to the rounding issue. Defs' Br. at 19-20. In those cases, the patentee attempted to broaden the *literal* scope of numerical claims to encompass more than ordinary rounding. For example, *Cobalt Boats* involved the claim term "180 degrees." 773 F. App'x 611, 616 (Fed. Cir. 2019). But the court never addressed rounding. Rather, the court rejected the plaintiff's attempt to *literally* encompass an accused product that rotated "between 172 and 179 degrees," holding that such a product did not literally infringe. *Id.* at 617. But this does not resolve the parties' dispute here, because the plain meaning of "180" using standard rounding practices would literally extend only down to 179.5 degrees, which was not argued for in *Cobalt Boats*.

In *Jeneric*, the court rejected the plaintiff's positions that 1.61% cerium oxide literally infringed a limitation reciting "0-1%," and that 15.97% aluminum oxide literally infringed a limitation reciting "7-15%." 205 F.3d 1377, 1382-83 (Fed. Cir. 2000). Both measurements were outside of standard rounding limits—"1%" would only extend to 1.4%, and "15%" would only extend to 15.4%. Lastly, the plaintiff in *Takeda* attempted to expand the scope of "400 μm or less"

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offer Dr. Thompson's testimony since April, when Plaintiffs served their Rule 4.2(c) disclosure. Defendants had the opportunity to submit their own expert testimony with their opening brief and chose not to.

to literally include 440 μm, far outside the scope of rounding for "400," which would only extend to 400.4. 743 F.3d 1359, 1363 (Fed. Cir. 2014). All of these cases involved arguments for numerical limits beyond ordinary rounding convention. These cases do not address the issue here—whether ordinary rounding rules apply—and are therefore inapplicable.

The Federal Circuit also squarely rejected Defendants' argument that rounding rules do not apply in the absence of broadening words such as "about." *Actelion Pharms. LTD v. Mylan Pharms. Inc.*, 85 F.4th 1167 (Fed. Cir. 2023). There, the defendant argued that the claim term "a pH of 13 or higher" had an absolute floor of 13. *Id.* at 1170. It argued that the absence of approximation language like "about," which was present in other claim terms, "must mean that 'a pH of 13' is exactly 13." *Id.* at 1171. The court rejected this argument and instructed: "[w]e reject any invitation to create a bright-line rule—either that language like 'precisely' or 'exactly' is always needed to avoid rounding or that the lack of approximation language, even when it may be found elsewhere in the claims, dictates a precise value." *Id.* (emphasis added). The lack of broadening language in claim 1 of the '359 patent thus does not preclude the application of ordinary rounding principles to determine claim scope.

2. Defendants' Lone Case Concerning Rounding Involved The Patentees' Effective Disclaimer Of Rounding

The only case cited by Defendants that discusses rounding is *AstraZeneca AB v. Mylan Pharms. Inc.*, 19 F.4th 1325 (Fed. Cir. 2021). Defs' Br. at 22-23. But in that case, the intrinsic evidence affirmatively showed that the patentee did not intend for standard rounding to apply to the claim term at issue, "0.001%." Applying the rules of standard rounding to 0.001% would have encompassed values as low as 0.0005%. However, the patent specification disclosed that formulations with "0.001%" PVP were superior to those with 0.0005% PVP:

> it is clear that the inventors understood that a formulation comprising **0.001%** w/w PVP is more stable than (**and indeed, different from**) a formulation with even a

> slight difference in the concentration of PVP, e.g., a formulation with **0.0005**% w/w PVP…the written description suggests that the claimed formulations with 0.001% w/w PVP were intended to be more exact

Id. at 1332 (emphases added). Because of the patent's express statements, the court declined to apply rounding.

The *AstraZeneca* decision turned on the fact that the patentee made clear and unmistakable statements that the claimed number (0.001%) was "indeed, different from" a number that would have been covered by rounding (0.0005%), and the court explained that its decision was premised on the specific context provided by the specification. *Id.* Here, the specification does not distinguish nucleic acid-lipid particles within the scope of rounding. For example, there is no disclosure stating that nucleic acid lipid particles with 50 mol % cationic lipid were superior to lipid particles with 49.5-49.9 mol % cationic lipid. The *AstraZeneca* case thus fails to support Defendants' position.

3. The Deletion Of The Word "About" During Prosecution Had Nothing To Do With Rounding

Defendants are wrong that the prosecution history excludes the application of the standard rules of rounding. Defs' Br. at 20-24. Defendants focus on the patentee's removal of the word "about" from the claims during prosecution of the '069 patent, ignoring the dispositive information showing why the amendment was made. Defs' Br. at 20-23. In a May 12, 2011 office action, the examiner rejected claims reciting "a cationic lipid comprising from about 50 mol % to about 65 mol %" as anticipated by the MacLachlan reference, which disclosed "2-60, 5-50, 10-45, 20-40, 30 mol %" cationic lipid. D.I. 84-3 Ex. 26 at 2, 4. The examiner stated that "'comprising about' could embrace an amount +/- 10, 20, 30 mol % of a lipid component." *Id.* at 2. The patentee then removed the word "about" specifically to avoid the +/- 10, 20, 30 mol % interpretation that the

examiner objected to, and in response the examiner allowed the claims. D.I. 84-3 Ex. 27 at 2; D.I. 84-3 Ex. 28.

To put this in perspective, the prosecution history involved the issue of whether the term "about 50" mol % encompassed a variation of **10, 20, and 30 mol %**, which would include a value as low as 20 mol %. The issue presented here is whether, based on standard rounding, the term "50" mol % literally encompasses values as low of 49.5 mol %, a variation of **0.5 mol %**. The stark difference makes plainly evident that the issue during prosecution had nothing to do with rounding.

As the court found in *Arbutus Biopharma Corp. v. Moderna, Inc.*, No. 22-CV-252, 2024 WL 1434526, at *11 (D. Del. Apr. 3, 2024) ("*Arbutus Delaware*"), when the patentee removed the phrase "comprising about," it "only clearly disclaimed these broader ranges and not the scientific conventions of rounding, which allow for minimal variation." The prosecution history unambiguously establishes that the examiner equated "about" with "+/- 10, 20, 30 mol %" and that the patentee removed "about" to overcome that interpretation. Defendants are thus wrong that the removal of "about" means that the patentee conveyed "strict numerical boundaries and excluded rounding." Defs' Br. at 21. None of the language from the prosecution history that Defendants cite concerns rounding. Defs' Br. at 20-23. Moreover, the patentee's statements characterizing the claimed ranges as "narrow" were merely in comparison to claims the examiner understood to permit a variation of "+/- 10, 20, 30 mol %."

The patentee's description of the invention's "unexpectedly superior advantages" also fails to exclude rounding from the claims, contrary to Defendants' arguments. Defs' Br. at 22. During prosecution, the patentee remarked:

> Applicants have found that SNALP formulations having increased amounts of cationic lipid, e.g., one or more cationic lipids comprising from 50 mol % to 65 mol

> % of the total lipid present in the particle, provide ***unexpectedly superior advantages*** when used for the *in vitro* or *in vivo* delivery of an active agent, such as a therapeutic nucleic acid (e.g., an interfering RNA).

D.I. 84-3 Ex. 27 at 9 (emphases in original). These statements fail to demonstrate that the patentee disclaimed rounding. Defendants again seek to confuse the issue. Plaintiffs are not attempting to broaden the term "50" beyond its plain meaning. The number "49.5" is within the plain meaning of "50" because when stated as two significant digits—as recited in the claims—the number "49.5" means "50." Thus, Plaintiffs' remarks show no departure from the plain meaning of the recited range, which as explained in detail in Plaintiffs' opening brief, means that significant figures and rounding apply. Pls' Br. at 16-19. As the *Arbutus Delaware* court explained, Plaintiffs would have used the term "50.0" had they intended more specificity:

> This interpretation of Plaintiffs' disclaimer is also consistent with Plaintiffs' finding of "unexpected results" within a narrower range, a range that exists even with the rules of rounding. Had Plaintiffs intended to add more specificity, they could have added additional significant figures, i.e. a mol % range of 50.0 to 65.0.

2024 WL 1434526, at *11.

The prosecution statements certainly do not provide "clarity" that the patentee intended to exclude rounding and do not provide support for the Defendants' claim construction position, much less the unambiguous support required for disclaimer. Defs' Br. at 24. The Court should adopt Plaintiffs' construction.

D. "Consisting Essentially Of" ('378 Patent)

Defendants assert that the "basic and novel properties" of the invention claimed by the '378 patent "include: increased activity of the encapsulated nucleic acid, improved tolerability of the formulations in vivo, significant increase in therapeutic index, and stable, **compared to lipid particles having less than 50 mol % cationic lipid**." Thus, Defendants' proposed construction for the "basic and novel properties" hinges on a comparison of the claimed particles with lipid

particles having "less than 50 mol % cationic lipid," a transparent attempt to read a 50% cationic lipid limitation into the claims that does not exist. Defendants attempt to justify their claim revision by asserting that Plaintiffs' specification disclaimed all embodiments with less than 50% cationic lipid. But the specification demonstrates otherwise—it identifies embodiments with less than 50% cationic lipid as being within the scope of the disclosed inventions. Adoption of Defendants' construction would improperly exclude these exemplary embodiments from the claims. The Court should therefore dismiss Defendants' disclaimer argument and reject Defendants' alleged "basic and novel properties" position on this basis alone.

Defendants' proposed construction is also flawed because the specification does not disclose, or even support, the comparison that Defendants propose for evaluating novel properties of the claimed particles. Defendants propose a comparison between the claimed particles on the one hand and particles with "less than 50 mol %" cationic lipid on the other. But the specification never suggests such a bright-line comparison and instead discloses that certain embodiments of the invention are advantageous as compared to "**compositions previously described**," which refer to compositions containing 30 and 40 mol % cationic lipid. 30 and 40% are of course below 50%, but there is no basis (*e.g.*, an express statement like that in *AK Steel*) for Defendants' importation of a "50 mol % cationic lipid" boundary into the claims.

Yet another problem with Defendants' argument is its reliance on statements directed to embodiments having a specified numerical cationic lipid limit rather than to the claimed invention, which does not recite such a numerical limitation for the cationic lipid. Defendants point to statements in the specification regarding embodiments of the invention that have "about 50 mol %" or more cationic lipid. These statements are thus irrelevant to the parties' claim construction dispute regarding a claimed invention—as in the case of the '378 patent—that does not recite a

numerical limitation for the cationic lipid. Defendants point to nothing else in the specification that identifies their proposed properties as the source of novelty for a claim reciting no numerical limitation for the cationic lipid. To the contrary, the prosecution history clearly shows that both the patentee and the examiner regarded the four-lipid combination and the recited molar ratios to be the novel properties of the claims that distinguished them over the prior art, and not any of the general characteristics proposed by Defendants.

Lastly, Defendants' criticism of Plaintiffs' proposed construction is unfounded. Plaintiffs' construction comports with the intrinsic evidence showing how the '378 claims were distinguished over the prior art. Contrary to Defendants' contention, it is not the case that Plaintiffs' proposed construction merely recites the claim elements. Plaintiffs' construction makes it clear that, for example, unlisted ingredients such as a fifth type of lipid are excluded from the scope of the claims.

1. Defendants' Proposed Construction Erroneously Reads Limitations Into The Claims

Defendants' proposed construction depends entirely on their erroneous attempt to read limitations into the '378 claims. Specifically, Defendants' proposed "basic and novel properties" require the claimed particles to show a comparative improvement in activity over particles with less than 50% cationic lipid, which implicitly **reads in** a requirement of "at least 50% cationic lipid" into the claims. Defendants are attempting to construct a bright-line infringement test, under which any particle having less than 50% cationic lipid—that meets all of the recited elements of the '378 claims—would automatically fall outside the scope of the claims because such a particle cannot have increased activity as compared to itself.

The fatal flaw in Defendants' proposed construction is that the '378 claims do not include any "50% cationic lipid" limitation and the intrinsic evidence does not support adding such a limitation to the claims. More specifically, element (b) of claim 1 of the '378 patent reads "a

cationic lipid having a protonatable tertiary amine," with no numerical limitation. Defendants recognize that the claim language is inconsistent with their position but maintain that "the specification is unequivocal enough to disclaim lower concentrations" of below 50% cationic lipid. Defs' Br. at 29. Not so. The specification expressly characterizes embodiments with less than 50% cationic lipids as part of the invention—there was no disclaimer at all, much less a "clear and unmistakable one." *Cont'l Cirs. LLC v. Intel Corp.*, 915 F.3d 788, 797 (Fed. Cir. 2019).

"It is a 'bedrock principle' of patent law that 'the claims of a patent define the invention.'" *Phillips*, 415 F.3d at 1320. Claim 1 of the '378 patent does not recite a limitation related to the mol % of the cationic lipid. By contrast, claim 1 and numerous dependent claims do recite explicit mol % limitations related to other lipid elements. *See* '378 patent, claims 2, 7, 13, 18, 24, 25, 29. This demonstrates that the patentee knew how to include lipid mol % limitations and chose not to do so for the cationic lipid component of the claim. *See Hill-Rom Services, Inc. v. Stryker Corp.*, 755 F.3d 1367, 1372 (Fed. Cir. 2014) (claims must "not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction"); *see also Helmsderfer v. Bobrick Washroom Equip., Inc.*, 527 F.3d 1379, 1383 (Fed. Cir. 2008) ("Courts do not rewrite claims[.]").

The claims of the '359 patent also underscore the fallacy of Defendants' argument. The '359 patent claims recite "a cationic lipid comprising from 50 mol % to 65 mol % of the total lipid present in the particle"—an express cationic lipid mol % limitation. "It is settled law that when a patent claim does not contain a certain limitation and another claim does, that limitation cannot be read into the former claim." *HW Tech., LC v. Overstock.com, Inc.*, 758 F.3d 1329, 1333 (Fed. Cir. 2014). That other patents' claims recite cationic lipid mol %—but the claims of the '378 patent do not—is dispositive. *E.g., Arlington Indus., Inc. v. Bridgeport Fittings*, 632 F.3d 1246, 1254-55

(Fed. Cir. 2011) (refusing to import "split" limitation recited in a claim of parent patent); *Eis, Inc. v. Intihealth Ger GMBH*, 2023 WL 346631, at *3 (D. Del. Jan. 9, 2023) ("connection element" should not be read into all claims, where it was recited in some patents but not others). Other claim language of the '378 patent further undermines Defendants' construction. *Phillips*, 415 F.3d at 1314 ("the claims themselves provide substantial guidance as to the meaning of particular claim terms"). Element (c) of claim 1 recites "a mixture of a phospholipid and cholesterol of from 30 mol % to **55 mol %** of the total lipid present in the particle." Defendants' proposed construction, which requires at least 50 mol % cationic lipid, would improperly truncate the upper limit (55 mol %) of the claimed mixture of phospholipid and cholesterol.

Nothing in the specification shows a disclaimer of embodiments with less than 50 mol % cationic lipid, as Defendants assert. To the contrary, the specification shows the opposite. The specification discloses that "[i]n some embodiments, the non-cationic lipid (e.g., one or more phospholipids and/or cholesterol) may comprise…about 55 mol %," which means that the cationic lipid could be lower than 50 mol %. *E.g.*, '378 patent, 20:19-34, 52:59-63. These disclosures confirm that, when the patentee claimed "a cationic lipid having a protonatable tertiary amine" without any accompanying language regarding the molar ratio of this lipid, the patentee did not intend to exclude compositions with less than 50 mol % cationic lipid from the scope of the claims or to require more than 50 mol % cationic lipid for all embodiments of its invention, as Defendants' proposed rewrite would do.

The court in *Arbutus Delaware* was presented with the issue of reading an "at least 50 mol %" cationic limitation into the '378 claims and declined to do so. 2024 WL 1434526, at *13. Regarding the '378 patent's specification, the court explained "Moderna's proposed requirement that the cationic lipid in the nucleic acid-lipid particle have at least 50 mol % is absent from the

claim language and is not present in the specification's description of the invention. To import that limitation from the preferred embodiments in the specification would run counter to well-established Federal Circuit law." *Id.* at *14. The Court here should dismiss Defendants' disclaimer argument for the same reasons and reject Defendants' proposed construction of the "basic and novel properties" on this basis alone.

Additionally, Defendants' attempt to read in a lower boundary of 50 mol % cationic lipid improperly conflates claim construction and infringement for "consisting essentially of" claim terms. Defendants argue that cationic lipid amounts less than 50 mol % "**materially alter** the basic and novel properties of the invention" and that "the basic and novel properties" "permit no less than 50 mol % cationic lipid." Defs' Br. at 29 (emphasis added). But whether something "materially alters" the basic and novel properties is a question of infringement, not claim construction. "Two questions arise when claims use the phrase 'consisting essentially of.' One question focuses on definiteness: what are the basic and novel properties of the invention? **The other question focuses on infringement**: does a particular unlisted ingredient **materially affect** those basic and novel properties?" *HZNP Medicines LLC v. Actavis Lab'ys UT, Inc.*, 940 F.3d 680, 695 (Fed. Cir. 2019) (emphases added). "Whereas ascertaining the basic and novel properties of an invention is a question of law, determining whether unnamed elements 'materially affect' these properties is a question of fact." *L'Oréal S.A. v. Johnson & Johnson Consumer Cos.*, No. 12-CV-98-GMS, 2014 U.S. Dist. LEXIS 190268 at *8-9 n.3 (D. Del. Nov. 5, 2014).

Defendants attempt to use the second question—what materially affects the basic and novel properties—as a basis for determining what those basic and novel properties are, which is the first question. *AK Steel Corp. v. Sollac & Ugine*, 344 F.3d 1234 (Fed. Cir. 2003), does not support Defendants' attempt to conflate the two questions. In *AK Steel*, the district court first held that

"good wetting is the goal of the invention as well as what distinguishes it from the prior art" and that the patentee drew a "precise line" from materials that "contain[] too much silicon and do[] not achieve that goal" based on an express statement in the specification that "[s]ilicon contents in the coating metal should not exceed about 0.5% by weight." *Id.* at 1239-40. The accused product in *AK Steel* contained 8-8.5% silicon, and the court granted summary judgment of non-infringement because "silicon in excess of 0.5% by weight would materially alter the basic and novel properties of the invention." *Id.* Here, the '378 patent does not teach that particles with less than 50% cationic lipid cannot achieve improved properties relative to prior compositions, such as those with 30% or 40% cationic lipid.

2. Defendants' Proposed Basic and Novel Properties of the Claimed Invention Are Not Supported by the Intrinsic Evidence

Defendants' proposed construction also conflicts with the intrinsic evidence in three other respects. First, the specification does not disclose the comparison that Defendants seek for their proposed "basic and novel properties." Second, Defendants rely entirely on a portion of the specification directed on its face to embodiments having a specified numerical limit for the cationic lipid, which the '378 claims do not recite. And third, Defendants ignore the prosecution history that clearly identifies the basic and novel properties for the '378 invention.

a. The Specification Does Not Disclose The Comparison That Defendants Propose

Defendants' proposal requires that the claimed particles have several benefits as "compared to lipid particles having less than 50 mol % cationic lipid." In so doing, Defendants contend that the specification teaches a bright-line rule that particles having 50% or more cationic lipid have superior properties to all particles having less than 50% cationic lipid. But the statement upon which Defendants rely does not support the comparison Defendants propose. The portion of the specification relied on by Defendants, Defs' Br. at 28, discloses:

> The present invention is **based, in part,** upon the surprising discovery that lipid particles comprising **from about 50 mol%** to about 85 mol % of a cationic lipid, from about 13 mol% to about 49.5 mol% of a non-cationic lipid, and from about 0.5 mol% to about 2 mol % of a lipid conjugate provide advantages when used for the in vitro or in vivo delivery of an active agent, such as a therapeutic nucleic acid (e.g., an interfering RNA). In particular, as illustrated by the Examples herein, the present invention provides stable nucleic acid-lipid particles (SNALP) that advantageously impart **increased activity** of the encapsulated nucleic acid (e.g., an interfering RNA such as siRNA) and **improved tolerability** of the formulations in vivo, resulting in a significant increase in the therapeutic index **as compared to nucleic acid-lipid particle compositions previously described**.

'378 patent at 6:13-21 (emphases added).

First, the specification fails to support the line Defendants attempt to draw because it makes clear that the invention is based only "in part" on the properties of "particles comprising from about 50 mol% to about 85 mol % of a cationic lipid…." Second, there is no bright line at 50 mol % cationic lipid because the above excerpt discloses particles having "from **about** 50 mol%...." And third, the specification's comparisons are to two specific "compositions previously described," ***not*** to all particles "having less than 50 mol % cationic lipid" as Defendants urge. For example, the portion of the specification immediately following the above excerpt teaches:

> As a non-limiting example, FIG. 3 of Example 4 shows that one SNALP embodiment of the invention ("1:57 SNALP") was more than 10 times as efficacious as compared to a nucleic acid-lipid particle **previously described ("2:30 SNALP")** in mediating target gene silencing at a 10-fold lower dose. Similarly, FIG. 2 of Example 3 shows that the "1:57 SNALP" formulation was substantially more effective at silencing the expression of a target gene as compared to nucleic acid-lipid particles **previously described ("2:40 SNALP")**.

'378 patent at 6:24-33 (emphases added). The "compositions previously described" correspond to only two embodiments, one containing 30% ("2:30 SNALP") and the other 40% ("2:40 SNALP") cationic lipid, '378 patent at 6:24-33, 75:11-16, Table 4. The specification does not equate the compared prior art with "having less than 50 mol % cationic lipid." Defendants' attempt to revise the specification should be rejected.

b. Defendants Cite To Nothing In The Specification Identifying The Basic And Novel Properties Of The '378 Patent Claims

Defendants' proposed construction should also be rejected because Defendants have not identified any statements from the specification that disclose the basic and novel properties of the invention of the '378 patent. To the contrary, Defendants rely on statements referring only to embodiments having a specified numerical limit for the cationic lipid. But the claims at issue here do not recite a numerical limitation for the cationic lipid. Those statements relied on by Defendants are thus inapplicable to the question of the basic and novel properties of the '378 patent invention. In determining the basic and novel properties, the question is "what distinguishes [the invention] from the prior art." *See AK Steel*, 344 F.3d at 1239-40. Thus, Defendants would need to identify statements in the specification that distinguish claims reciting no numerical limitation for the cationic lipid. Defendants identify nothing in the intrinsic evidence that suggests the claimed invention of the '378 patent—reciting no numerical limitation for the cationic lipid—was distinguished from the prior art based on "increased activity," "improved tolerability" or "increase in therapeutic index."

Defendants have not identified any statements in the specification indicating the novel properties of the invention claimed in the '378 patent. Defendants certainly point to nothing in the specification that distinguishes the invention of the '378 patent over the prior art based on characteristics of "increased activity," "improved tolerability," or "increase in the therapeutic index." Nor do Defendants allege that Plaintiffs relied on such characteristics to distinguish the claims of the '378 patent over the prior art during patent prosecution.

The facts here are thus different from those in *AK Steel*, 344 F.3d at 1239, and *HZNP*, 940 F.3d at 695, where the patents clearly disclosed what the properties were for the claimed invention at issue. In *AK Steel*, the "specification clearly state[d] that good wetting is the goal of

the invention **as well as what distinguishes it from the prior art**." 344 F.3d at 1239 (emphasis added). Here, by contrast, the claims of the '378 patent recite amounts for other lipid types but not for the cationic lipid. Defendants cite nothing from the specification that distinguishes this invention over the prior art based on the characteristics cited by Defendants. And in *HZNP*, the specification identified the basic and novel properties "by separate subheadings in the section titled 'Characteristics of the Gel Formulation.'" 940 F.3d at 693. Each of the basic and novel properties had their own subheading and there was no evidence that the properties did not apply to the full scope of the invention as claimed. *Id.* Defendants point to no such statements in the specification of the '378 patent that is applicable to the scope of the invention claimed in the '378 patent.

The '378 patent does not discuss "increased activity," "improved tolerability," and "increase in the therapeutic index" or "stability" as being the sole, limiting, novel characteristics of an invention having the scope of the '378 claims with no recited numerical limitation for the cationic lipid. Thus, those characteristics cannot define the basic and novel properties of the invention. *See also Aventis Pharma S.A. v. Hospira, Inc.*, 743 F. Supp. 2d 305, 357-58 (D. Del. 2010) ("stability is not required in the claims, and certainly is not discussed in the patents as a novel characteristic of the alleged invention").

c. Defendants' Construction Is Inconsistent With The Intrinsic Evidence From The Prosecution History

Defendants' proposed construction fails to take into account how the '378 invention actually was identified as novel over the prior art. Plaintiffs explain in detail in their opening brief that the combination and concentration of the lipid components is how the patentee distinguished the claims during prosecution. Pls' Br. at 26-27. The patentee repeatedly emphasized that the prior art did not include "a four component lipid particle," or other lipid components at the recited concentration ranges. *Id.* Those are the basic and novel properties that distinguished the prior art.

The situation here is similar to *Aventis*, 743 F. Supp. 2d 305, and *L'Oréal*, 2014 U.S. Dist. LEXIS 190268, at *6-7 n.2, where the court relied on the prosecution history to determine the basic and novel properties. The prosecution history for the '378 patent clearly shows that the invention was novel over the prior art based on a four-lipid system with the recited ratios. Plaintiffs' proposal for the basic and novel properties considers how the invention was actually characterized as being novel, which is the point of the inquiry. *See AK Steel*, 344 F.3d at 1239-40.

3. Defendants' Criticisms Of Plaintiffs' Construction Are Unfounded

Defendants are wrong that claim elements cannot be the basic and novel properties of an invention. Defs' Br. at 30. Courts regularly determine the basic and novel properties based on the claim elements. In *PPG Indus. v. Guardian Indus. Corp.*, the claim at issue recited a "green tinted, ultraviolet absorbing glass having a base glass composition consisting essentially of" several compounds at particular ranges, and "a colorant portion consisting essentially of" other compounds at recited amounts. 156 F.3d 1351, 1352 (Fed. Cir. 1998). The court did not disturb the parties' agreement that "the basic and novel characteristics of the glass are **color, composition**, and light transmittance." *Id.* at 1354 (emphasis added). Similarly, in *Aventis*, the claims required that "the docetaxel be 'dissolved' in **polysorbate 80** and (in the case of the '561 Patent) ethanol," and the court determined that "the use of **polysorbate 80** as the sole surfactant is a basic and novel property of the invention[.]" 743 F. Supp. 2d at 357-58 (emphases added). And in *L'Oréal*, 2014 U.S. Dist. LEXIS 190268, at *1, *6-7 n.2, the court ruled that the "basic and novel property of the claimed invention is stabilizing avobenzone with respect to ultraviolet radiation by adding a specified amount of octocrylene" where the claims at issue "recite processes 'for stabilizing [avobenzone]' by adding specified amounts of octocrylene to a cosmetic screening compound containing avobenzone." *Id.* (alteration in original).

Defendants are also wrong that Plaintiffs' "basic and novel properties" simply recite the claim language and that "the claim scope is, effectively, as broad as an open-ended 'comprising' claim." Defs' Br. at 30. Because the number and relative concentrations of lipid components are the basic and novel properties, any particle with an unrecited ingredient that materially alters those properties would be outside of the claim. The prosecution history is clear that the claims are limited to a "four component lipid system." Pls' Br. at 26-27. A particle containing a fifth type of lipid would materially affect the basic and novel property of the combination of lipid components (i.e., only four types) and thus would be excluded from the scope of the '378 claims based on the "consisting essentially of" language. In contrast, a "comprising" claim could encompass such an embodiment. Plaintiffs' construction is consistent with the patentee and examiner's understanding of the basic and novel properties of the claimed invention as a whole. The Court should reject Defendants' proposed construction for "consisting essentially of," and instead adopt Plaintiffs' construction.

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Respectfully submitted,

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